Asian Journal of Basic Science & Research
Volume 6, Issue 2, Pages 183-194, April-June 2024

Formulation and Evaluation of Iodine Transdermal Patch for Women of Reproductive Age

Akanksha Tiwari[1*], Dr.M.Alagusundaram[2], Namrata Mishra[3], Vijeta Bhattacharya[4], Priyanka Keshri[5] & Anantika Rahi[6]

[1-6]*School of Pharmacy, ITM University, Turari, Gwalior, Madhya Pradesh, India.*
Corresponding Author Email: akankshaaniruddh@gmail.com[*]

DOI: http://doi.org/10.38177/AJBSR.2024.6214

Article Received: 14 April 2024 *Article Accepted: 26 June 2024* *Article Published: 29 June 2024*

ABSTRACT

Iodine deficiency is today's time the leading cause of brain damage not just in India but around the globe, IDD are along with a host of other health complications. Most Iodine Deficiency Disorders are often both invisible and irreversible but at the same time, these are largely preventable. Indian, population is at a greater risk as the soil covering the Indian landmass lacks iodine, therefore the crops grown are also devoid of this element. Iodine-fortified salt mitigates the risk however this cannot compensate for the daily requirement of iodine in women, especially in the vulnerable rural areas of India. Transdermal drug delivery can be simply described as the method of transporting drug molecules across the skin via preformulated patches. These patches stick to the surface of the skin which absorbs the drug molecule and passes it to the bloodstream for further transport. The research aims to develop an alternative means for women in rural India to be equipped with the daily dose required of Iodine by applying a self-adhesive transdermal patch in the form of bindis with an iodine solution.

Keywords: Iodine; Skin; Patches; Iodine deficiency disorders; Transdermal drug delivery system; Bindi; Preformulated; Goitre; Hyperthyroidism; Permeation enhancers; Epidermis.

1. Introduction

Transdermal drug delivery can be best characterized as the technique of transferring medication molecules over the skin. As a consequence the epidermis provides a wide surface area for medication absorption and is one of the most easily accessible organs in the human body. Transdermal drug delivery systems (TDDS) take use of the skin's relative ease of access. Transdermal medication administration skips the enterohepatic circulation, enabling more consistent therapeutic activity. Transdermal patches are adhesives that cling themselves to the skin and deliver medications or liquids via the epidermis after sustained skin contact. An adhesive binds the patch to the skin, and after a while, the transdermal solution seeps past the skin cells and into the dermis for further circulation in the body. Rather from taking a pill or getting an injection, drugs are increasingly being designed for transdermal use. Convenience, consistency, easier dosage, less digestive side effects, and improved patient experience are just a few of the benefits of administrating drug via TDDS. The most popular transdermal patches are nicotine patches. Other examples include therapies for Vitamin C insufficiency, CBD delivery, ADHD treatments, hormone deficit, nausea alleviation, and even scent delivery or insect repellent transdermal patches. Transdermal patches serve a number of purposes, including another way of providing medications, nutrition, or other substances. Iodine shortage is the prevalent cause of brain damage worldwide, as well as a variety of other health issues. In India, the biggest challenge is that the soil has very low quantities of iodine thus the crops grown also suffer iodine deficiency. Iodine-fortified salt reduces the risk, though it cannot provide the daily iodine requirements of women, particularly in rural parts of India where women are at a greater risk of iodine deficiency [1-7].

1.1. Study Objectives

1. The main objective of the study is to design and evaluate the Iodine Transdermal patches in the form of Bindi which can be worn by women daily.

2. This present investigation was to prepare Transdermal Iodine patches using adequate polymers, evaluate the patch, and study the drug release via the skin into the bloodstream.

3. The concept of TDDS is to deliver the patient with non-conventional means of attracting their medication.

4. Drugs are absorbed from the skin and then reach the nerves for further systemic circulation as saliva permits down into the stomach.

5. In this current study effort will be made to formulate a patient friendly dosage form of TDDS of iodine.

6. The TDDS have the property of constant release of drug as they come in contact with the skin.

1.2. Reasons to Choose Patches

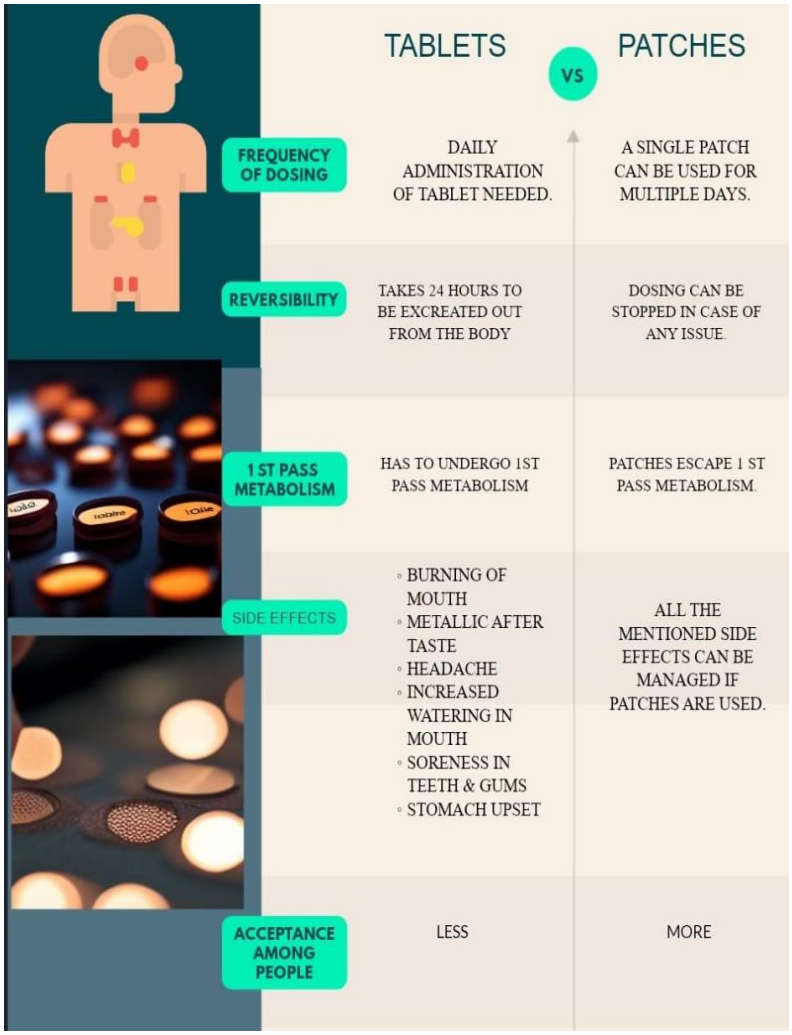

Figure 1. Reasons to choose a patch

1.3. Iodine – a necessity for women

Iodine status differs in men and women, and iodine deficiency has more severe consequences for women as it will affect future generations.

Iodine is essential for women's health, particularly for thyroid function and fetal development during pregnancy. Here are some key points about iodine for women:

1. **Pregnancy and lactation**: Iodine is crucial for fetal brain development and growth. Pregnant and breastfeeding women need more iodine (220-290 mcg/day) to support their own thyroid function and their baby's development. Women should ideally be provided with iodine intake of at least 150 µg/day for a long period pre conception to ensure plentiful intrathyroidal iodine stores and adequate iodine supply during pregnancy.

2. **Thyroid health**: Iodine is necessary for the production of thyroid hormones, which regulate metabolism, energy, and other bodily functions. Women with thyroid issues, such as hypothyroidism, may need iodine supplements.

3. **Menstrual health**: Iodine may help alleviate menstrual cramps, bloating, and breast tenderness due to its anti-inflammatory properties.

4. **Breast health**: Iodine has been shown to have a protective effect on breast tissue and may help reduce the risk of breast cancer.

5. **Food source**s: Include iodized salt, seaweed (like kelp, dulse, or wakame), dairy products, and some fortified foods in your diet to meet your daily iodine needs.

6. **Fetal development**: Iodine deficiency during pregnancy can lead to cretinism, a condition causing mental retardation, deafness, and physical disabilities in children.

7. **Postpartum thyroiditis**: Iodine may help prevent or manage this condition, which causes thyroid inflammation and hormonal imbalances after childbirth.

8. **Menopausal symptoms**: Iodine may alleviate hot flashes, night sweats, and mood swings due to its role in regulating thyroid hormones.

9. **Polycystic ovary syndrome (PCOS):** Iodine may help manage PCOS symptoms, such as irregular periods, weight gain, and acne, by supporting thyroid function.

10. **Breastfeeding support**: Iodine is essential for breast milk production and infant development, making it crucial for breastfeeding women [8-10].

Table 1. RDA of Iodine

S. No.	Individual	RDAs
1	Infant	50 mcg/day
2	Children [1-8 years]	90 mcg/day
3	Children [9-13 years]	120 mcg/day
4	Adults	150 mcg/day
5	Pregnant women	220 mcg/day
6	Breastfeeding women	290 mcg/day

1.4. Status of Iodine amongst Women in India

The National Iodine and Salt Intake (NISI) research on carried out during 2014–15, was the first survey to assess the iodine status of women of reproductive age (WRA). A mUIC of 158 µg/L17 meant the iodine level was thought to

be sufficient. Even women of reproductive age who consumed non-iodized salt (mUIC: 112 µg/L) and poorly iodized salt (mUIC: 123 µg/L) in their households had superb iodine status, contrary to the learning, suggesting that iodine consumption may have been determined by cooked foods containing iodine. The 2018–19 India Iodine Survey determined that women of sexual maturity had the ideal iodine intake of 178 µg/L. This examination of iodine status was made again. Pregnant and nursing women were also found to have low iodine status (mUIC of both demographic groups was 173 µg/L) in this survey. This iodine status has been noted for all six zones of the nation as well as for all age groups the divisions based on the wealth index.

Over time, India's iodine status has now been better mostly due 24 24 19 to gains in coverage (more families ingesting salt that has been effectively iodized) and quality (more salt being iodized within the prescribed limits).In addition to the fact that nurse moms are at risk of iodine shortage, their well-being matters most since it maintains the health and well-being of their new-borns. While historically connected to poor countries, iodine deficiency may impact both developing and industrialized nations. More critically, in certain countries where iodine was previously accessible, the ion shortage has lately started to resurface. According to recent research, a decline in milk intake in the UK can be the cause of an absence of iodine among various groups in the country, such women who are pregnant, nursing, and of reproductive age. Iodine insufficiency has also been found to be recurrent in the same way in other European countries, particularly Finland, Italy, Hungary, France, Belgium, and Spain [11-13].

1.5. IDD Policy Development and Milestones in India [14]

Table 2. IDD Policy Development and Milestones

1990	The United Nations World Summit for Children and the World Health Assembly codified efforts to eliminate IDD.
1991	The Conference on Ending Hidden Hunger adopted the ambitious goal of virtually eliminating IDD as a public health problem by the turn of the century.
1993	The WHO reaffirmed the utility of salt iodization and proclaimed this as the key strategy to achieving this goal.
2007	The International Child Development Steering Group identified iodine deficiency as 1 of the 4 key global risk factors for impaired child development where the need for intervention remains urgent.

2. Method of Preparation

Solvent Casting Method

Twelve-well plates with a 2 cm diameter have been chosen for this purpose. PVA and PVP polymers were precisely measured, combined in 10 mL of water conjunction, and reduced from 70 percent ethyl alcohol to generate an ethanol solution with various volume percentages. The mixture was then set aside to produce a clear solution. The aforementioned solution was combined with the active ingredient (10 w/w%) until a clear solution was obtained. Propylene glycol and PEG 400 were utilised as plasticizers. The uniform solution that produced was then cast into

the plates and dried for predefined periods of time at 40 °C. The dry sections have been studied in greater detail from multiple perspectives [15].

Iodine Transdermal Patch Formulation

Technique used: Solvent casting.

Material used

Table 3. Materials used

S. No.	Name of Ingredients	Category
1	Iodine	Drug
2	Ethyl Cellulose	Backing Membrane
3	Propylene Glycol	Plasticizer
4	Polyvinylpyrrolidone	Polymer

General Procedure for Preparation of Iodine Transdermal Patch

The Iodine Transdermal patches were prepared by solvent casting technique. Various polymers were used as a film-forming polymer.

1. Measure the required polymer to be mixed in suitable solvent.

2. Plasticizer was mixed to the solution slowly with constant stirring in a clockwise direction and mixed by the use of magnetic stirrer.

3. Measured quantity of Iodine was mixed in 10 ml of solvent.

4. 2% Iodine soln. was put drop by drop to prepared solution of polymer & plasticizer, and mixed uniformly until a uniform consistency is achieved.

5. The preparation was rested for 24 hrs in order to remove any air bubbles.

6. The mixture was further casted on petri plate and dried overnight to get the film.

7. After that, the film was carefully taken out and sliced to the right size.

8. Prepared patch was packed in a sterilized packing to avoid contamination.

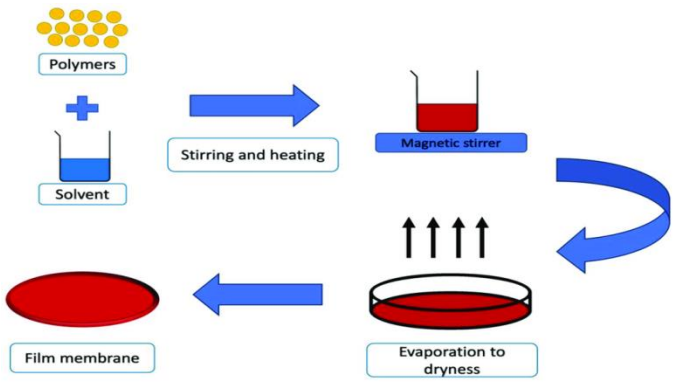

Figure 2. Schematic Diagram of the process

Asian Journal of Basic Science & Research
Volume 6, Issue 2, Pages 183-194, April-June 2024

3. Formulations

Lab Work

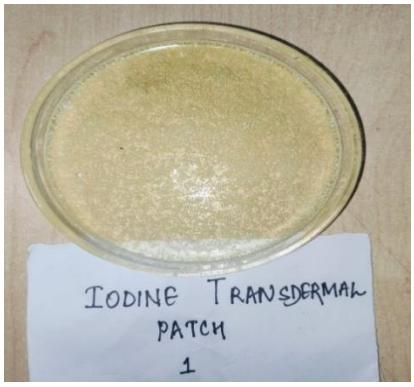

Figure 3. F1 batch

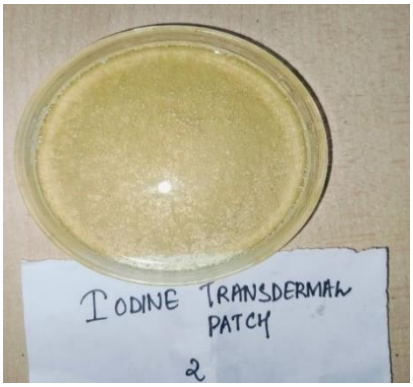

Figure 4. F2 batch

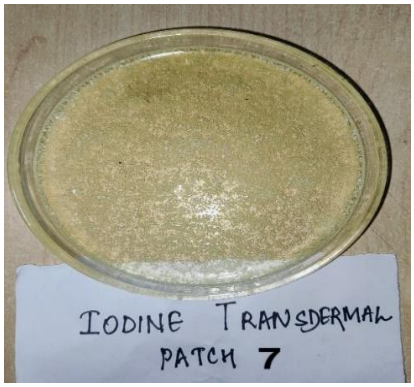

Figure 5. Optimized F7 Batch

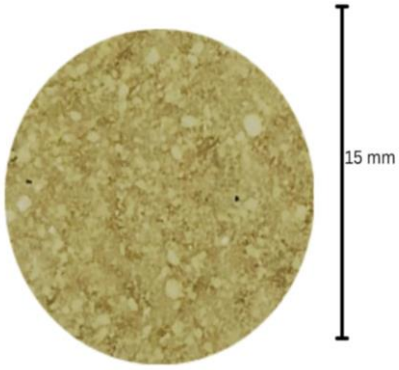

Figure 6. Bindi cut from F7batch

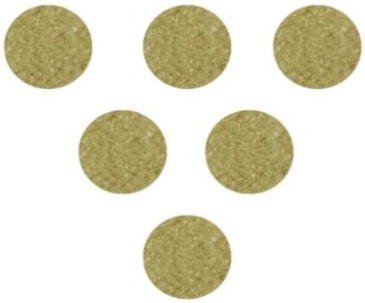

Figure 7. Before Dying

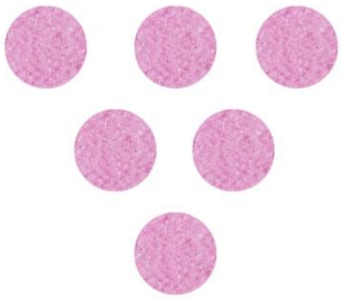

Figure 8. After Dying

Evaluation Parameters:

1) Weight of Patch

2) Patch Thickness

3) pH of Surface

4) Folding Endurance

5) Stability studies

6) Assay of Iodine Patch

7) Content Uniformity

8) Moisture absorption/water vapor absorption %age:

9) % moisture content

10) Skin irritation test

4. Preformulation Studies

A. Description of sample

Table 4. Description of sample

S. No.	Identification Test	Observation
1	Appearance	Crystalline
2	Odour	Metallic
3	Color	Violet

B. Solubility of Iodine Sample

Table 5. Solubility of Iodine Sample

S. No.	Solvent	Observed Solubility
1	Water	12.1 mg/ ml
2	Ethanol	34.2mg/ ml
3	Phosphate buffer pH 7.2	13.41 mg/ ml

C. Melting Point

Table 6. Melting Point

S. No.	Method	M.P Reported	M.P Theoretical
1	Digital melting point meter	114.0° C	115C°
2	DSC	115°C	115C°

D. Iodine sorption studies

Molecular iodine hydrolyzes in which water results in the existence of several iodine species the aqueous solution such as I^-, I_2, I^- and HOI. The possible bindings of PVP with different iodine species.

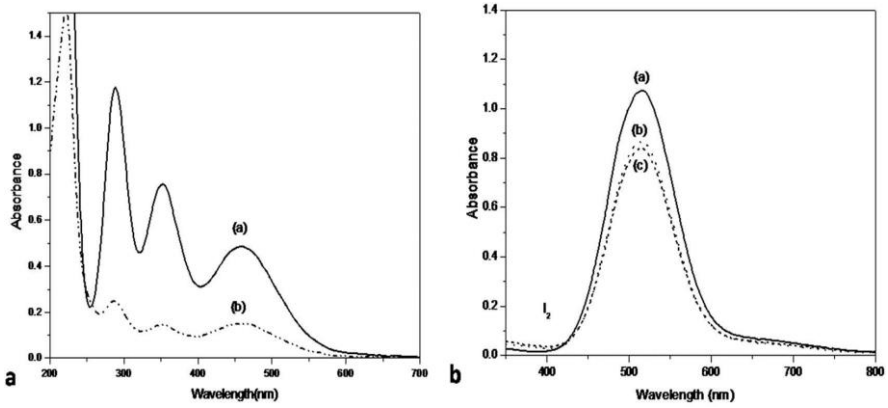

Figure 9. UV-Vis spectra of water containing dissolved molecular iodine initially

5. Results

A. Skin Irritation Test

Table 7. Skin Irritation Test Results

Rabbit No.	Reaction	Standard		Test	
		24 hours	72 hours	24 hours	72 hours
1	Erythema	+ +	+ + +	-	-
	Edema	+	++	-	-
2	Erythema	+	++	-	-
	Edema	++	+++	-	+
3	Erythema	+	++	-	-
	Edema	++	++	-	-
4	Erythema	++	+++	-	+
	Edema	+	+++	-	-
5	Erythema	++	+++	-	-
	Edema	+	++	-	-

B. Evaluation Parameters of TDDS

Table 8. Evaluation Parameters Result

Code	Average Weight (mg)	Thickness (mm)	Folding Endurance	Content Uniformity
F1	35.0± 0.1	0.49±0.04	135±5	99.64±4
F2	52.4±0.3	0.50±0.03	138±6	99.49±3

F3	53.0±0.3	0.48±0.04	141±4	101.67±4
F4	36.4±0.2	0.51±0.04	151±3	99.98±3
F5	42.2±0.1	0.50±0.03	155±5	98.86±4
F6	48.9±0.2	0.52±0.03	159±3	100.86±1
F7	38.3±0.2	0.54±0.05	162±6	99.50±4
F8	48.6±0.1	0.55±0.04	165±7	101.18±2

Code	**Surface pH**	**Flatness Percentage**	**Degree of Swelling**	**% Erosion**
F1	6.8±0.1	97±2	2.0±0.3	7.54±0.35
F2	6.8±0.2	97±2	2.1±0.4	7.59±0.42
F3	6.8±0.2	97±1	2.38±0.3	10.32±0.12
F4	7.0±0.3	98±2	2.51±0.2	16.29±0.15
F5	6.8±0.1	96±0	2.29±0.4	15.66±0.35
F6	6.8±0.2	97±2	3.71±0.3	18.70±0.34
F7	6.8±0.1	99±1	2.85±0.3	18.04±0.41
F8	6.8±0.2	98±1	2.74±0.2	15.17±0.31

6. Result and Discussions

All drug incorporated patches had been determined to be quite similar in thickness. The transdermal patches fluctuated in thickness from 0.322±0.008 to 0.484±0.012 mm, as presented. The batch thickness was found to be unusually high in F8, and low in formulation F3. This outcome of measurements revealed that the polymer's thickness is determined by its solubility and concentration. It implies that using the appropriate polymer is a necessary step in constructing a patch of optimal thickness, which might slow the release of the medication from the patch.

i. The TDDS formulation batches ranged in weight from 35.0±0.1 to 53.0±0.3 mg, while the content homogeneity was consistently between 98.86±4.08% and 101.67±4.78%.

ii. Minimal standard deviation values in the patch guarantee that the patches created using the solvent evaporation process are uniform. The drug content of all formulations demonstrated that the technique used to make patches in this investigation could produce patches with consistent drug content with little patch variability. All of the data suggested that the patches were uniform, as indicated by the standard deviation value.

iii. Each batch was examined for folding endurance. It fluctuates between 135±5 and 165±7. The folding endurance was found to be greater than 135, indicating that the prepared patches could tolerate mechanical pressure while remaining flexible.

iv. The PVP formulations and polymer concentrations have a very significant impact on folding endurance .The batch of ethyl cellulose, polyvinylpyrrolidone, and propylene glycol exhibited the expected filmforming properties.

v. The effects of polyvinylpyrrolidone and propylene glycol on total drug release and patch folding endurance were explored. Patches of formulation F7 had higher drug release, penetration, and in vivo absorption than patches from other formulations which fulfilled the physical evaluation standards.

vi. As a result, formulation F7 was chosen for additional comparison studies. Other patches formulations demonstrated greater drug release, in vitro penetration, and in vivo absorption than patches of other formulations. So, the formulations F7, which contained 3.0 gram of ethyl cellulose, 2.0 gram of polyvinyl pyrrolidone, and 5.0 ml of propylene glycol, were deemed to be the optimum formulations.

vii. It came to light that increasing the content of propylene glycol and polyvinyl pyrrolidone in the formulation results in prolonged drug release, greater in vitro permeation, and higher percentage drug release.

viii. It is possible to make an iodine transdermal patch utilizing ethyl cellulose, polyvinyl pyrrolidone as a film forming polymer, and propylene glycol as a plasticizer and penetration enhancer.

ix. Finally, it can be inferred that the transdermal drug delivery of Iodine Patch may be accomplished and prove that in-vivo study and skin irritation study, in vitro permeability, in vitro drug release, using a transdermal patch created by employing Ethyl Cellulose, Polyvinylpyrrolidone, and Propylene Glycol.

7. Conclusion

The project aimed towards creating an iodine transdermal device leveraging a polymer-matrix layered film. This enables one to adjust the overall release of the medicinal product by selecting the proper polymers and their mixes, along with incorporating the many different diffusion channels formed by the polymer blend to achieve the ultimate desirable steadiness and sustained drug release from the prepared patches. Thus, molecular diffusion via the polymer matrix provides an efficient, effortless, and trustworthy method for achieving sustained/controlled release of a wide range of active substances from the TDDS. The research identified and executed the appropriate percentage of the selected polymers, as well as the solvent ratio and manufacturing conditions. The project aimed towards creating an iodine transdermal device leveraging a polymeric matrix film. This enables one to adjust the overall release of the medicinal product by selecting the proper quantities of polymers and their mixes, along with incorporating the many different diffusion channels formed by the polymer blend to achieve the ultimate desirable steadiness and sustained drug release from the prepared patches. Thus, molecular diffusion via the polymer matrix provides an efficient, effortless, and trustworthy method for achieving sustained/controlled release of a wide range of active substances from the TDDS. The research identified and executed the appropriate percentage of the selected polymers to the solvent ratio and manufacturing conditions. By combining the most optimum composition, we were able to boost the bioavailability of iodine. In vitro drug release and permeation experiments revealed that the formulation is acceptable for the active substance's transdermal administration. This study permits and supports transdermal delivery of iodine, which is an essential and promising approach given its indication area. The study's findings provide a sensible guideline for developing an iodine transdermal treatment system for successful therapy

in women, supplying them with a suitable amount of iodine to fulfill their daily demands while also lowering their risks of developing IDD.

8. Future Suggestions

- Future research should focus on optimizing drug formulations, enhancing permeation techniques, and improving patient adherence to treatment regimens also gold standards must be set for TDDS formulation.
- The integration of novel nanotechnologies and advanced materials science will further revolutionize TDDS, making it a cornerstone in the treatment of skin diseases.
- It also highlights the challenges associated with TDDS including skin irritation, safety issues and lack of proper standardization for the manufacturing.

Declarations

Source of Funding

This study did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing Interests Statement

The authors declare no competing financial, professional, or personal interests.

Consent for publication

The authors declare that they consented to the publication of this study.

Authors' contributions

All the authors took part in literature review, analysis and manuscript writing equally.

Availability of data and material

All data pertaining to the research is kept in good custody by the authors.

References

[1] Prausnitz, M.R., & Langer, R. (2008). Transdermal drug delivery. Nat Biotechnol., 26(11): 1261–8. doi: 10.1038/nbt.1504.

[2] Hatch-McChesney, Adrienne & Harris R. Lieberman (2022). Iodine and Iodine Deficiency: A Comprehensive Review of a Re-Emerging Issue. Nutrients, 14(17): 3474.

[3] Ingibjörg Gunnarsdottir & Lisbeth Dahl (2012). Iodine intake in human nutrition: a systematic literature review. Food & Nutrition Research. https://pubmed.ncbi.nlm.nih.gov/23060737/.

[4] Abuladze, Nino, Ketevani Gabunia, Nato Alavidze, Natia Chubinidze & Irma Kikvidze (2022). Some issues in the development of a new type of iodine-containing pharmaceutical products.

[5] Dela Cruz, F., Brown, D.H., Leikin, J.B., Franklin, C., & Hryhorczuk, D.O. (1987). Iodine absorption after topical administration. West J Med., 146(1): 43–5.

[6] Patrick, J.S., & Yashveer, S. (2010). Martin's Physical Pharmacy and Pharmaceutical sciences. Sixth Edition, First Indian Reprint Published by Wolters Kluwer, New Delhi, India.

[7] Udhumansha, U.M., & Reddy, V.S. (2007). Transdermal Therapeutic System of Carvedilol: Effect of Hydrophilic and Hydrophobic Matrix on In Vitro and In Vivo Characteristics. AAPS Pharm Sci Tech.

[8] Asija, R., Kumar Preeti, K., Ajay, K.G., Preeti, V., & Pratiksha, J. (2012). Formulation and evaluation of matrix type transdermal patch of Atrovastatin calcium. Journal of Biomedical and Pharmaceutical Research.

[9] Fabian Nalluri, P.L., & Prashanth, R. (2014). Formulation and evaluation of drug in adhesive transdermal patches of Rivastigmine. Indo American Journal of Pharmaceutical Research.

[10] Eunjae, J., Eun, Y., & Lee (2015). Development of drug-in-adhesive patch formulations for transdermal delivery. https://pubmed.ncbi.nlm.nih.gov/25863117/.

[11] Jagtap, S.B., et al. (2017). In vitro and in vivo evaluations. International Journal of Pharmaceutics.

[12] Ashok, K.J., & Nikhila, P. (2010). Transdermal Drug Delivery System: An Overview. International Journal of Pharmaceutical Sciences Review and Research.

[13] Vijaya R., & Pratheeba, C. (2015). Study of the hydroxyl methyl cellulose combination in the development of transdermal film for amitriptyline HCl and their invitro characterization. International Journal of Pharmaceutical, Chemical and Biological Science, 5(3): 548–556.

[14] Arora, P., & Biswajit, M. (2002). Design, Development, Physicochemical, and In Vitro and In Vivo Evaluation of Transdermal Patches Containing Diclofenac Diethylammonium Salt. Journal of Pharmaceuticals Science.

[15] Mathur, V., & Satrawala, Y. (2010). Physical and chemical penetration enhancers in transdermal drug delivery system. Asian Journal of Pharmaceutics.